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Global and Regional Left Ventricular Circumferential Strain during Incremental Cycling and Isometric Knee Extension Exercise

Running title: Circumferential strain during exercise

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ABSTRACT

Background: The objective of this study was to investigate left ventricular (LV) circumferential strain responses to incremental cycling and isometric knee extension exercises.

Methods: Twenty-six healthy male participants (age= 30 ± 6 years) were used to study LV global (GCS) and regional circumferential strain at the apex (ACS) and base (BCS) during incremental cycling at 30% and 60% work rate maximum (W_{\max}) and short duration (15s contractions) isometric knee extensions at 40% and 75% maximum voluntary contraction (MVC) using two-dimensional speckle-tracking echocardiography.

Results: During cycling (n=22), GCS increased progressively from rest to 60% W_{\max} ($-22.85 \pm 3.26\%$ to $-29.87 \pm 2.59\%$, $p < 0.01$). ACS increased from rest to 30% W_{\max} ($-26.29 \pm 4.84\%$ to $-36.84 \pm 6.94\%$, $p < 0.01$) and then remained unchanged to 60% W_{\max} ($-40.72 \pm 4.06\%$, $p = 0.068$). BCS decreased from rest to 30% W_{\max} ($-19.41 \pm 2.79\%$ to $-17.51 \pm 4.66\%$, $p = 0.05$) then remained unchanged to 60% W_{\max} . During isometric knee extension (n=23), GCS decreased from rest to 40% MVC ($-22.63 \pm 3.46\%$ to $-20.10 \pm 2.78\%$, $p < 0.05$), then remained unchanged to 75% MVC. Similarly, BCS decreased from rest to 40% MVC ($-19.21 \pm 2.58\%$ to $-13.55 \pm 3.45\%$, $p < 0.01$) and then remained unchanged, whereas ACS did not change with exercise intensity (rest, $-26.05 \pm 5.34\%$; 40% MVC, $-26.64 \pm 4.53\%$ and 75% MVC $-27.22 \pm 5.34\%$, all $p > 0.05$).

Conclusion: GCS increased stepwise during incremental cycling, mediated by the apex with trivial changes at the base. In contrast, GCS decreased during the isometric knee extension to 40% MVC then plateaued, due to decreased BCS since ACS was maintained. A novel finding is that the GCS response appears to be exercise modality dependant and are the consequence of region-specific changes.

Keywords: exercise; deformation; left ventricle; speckle tracking echocardiography; strain

1. INTRODUCTION

Myocardial strain mechanics are used as markers of left ventricular (LV) function ¹, and are assessed in three planes of motion; radial, longitudinal and circumferential ². Circumferential strain reflects the change in length around the LV perimeter and during systole as the myocardium shortens leading to a reduced circumference of the LV cavity ^{3,4}. The healthy heart demonstrates a basal-to-apical gradient in circumferential strain, with higher strain in the apex, which highlights the non-uniform distribution of shortening about the long-axis of the ventricle ⁵.

Assessment of cardiac strain during exercise stress provides important information pertaining to the physiological capabilities of the LV to alter its function in response to an increased cardiac demand. Interrogation of circumferential strain during exercise will add additional knowledge regarding LV shortening during contraction, supplementary to the previously reported longitudinal strain during dynamic and isometric exercise ^{6,7}.

During incremental dynamic exercise, studies reported a plateau ⁸ or progressive increase ⁶ in global circumferential strain (GCS). Still, Doucende et al. ⁶ did not observe a statistically significant increase between final work intensities, making it difficult to determine whether at 40% maximal workload, GCS begins to plateau thereafter or larger workload increments are necessary to elicit notable differences between exercise intensities. Further, circumferential shortening during exercise also show regional disparity between apical and basal planes, with increases at the apex (ACS) without changes at the base (BCS) ^{9,10}, which however, contrasts another investigation having reported a reserve in BCS compared with baseline ¹¹.

Data pertaining to circumferential strain during resistance exercise are limited. Reductions in GCS were noted during isometric hand-grip exercises ¹³, however, regional strains were not independently reported. In contrast, more recently short-duration double-leg

press transiently reduced BCS and ACS¹³. Although, this was not traditional resistance exercise, since image acquisition was performed during an isometric hold following a brief near-complete leg extension. Therefore, the global and regional circumferential strain responses during incremental short-duration resistance exercise concerning sustained isometric work of the lower extremities remains to be determined.

Taken together, despite the aforementioned reports of circumferential strains during exercise, a full description, within the same investigation, of global and region-specific circumferential strains during incremental exercise are lacking at present and the responses during dynamic and static modalities remain incompletely understood. Also, there is some confusion in the literature regarding the effect of exercise on the different levels of the LV at which circumferential strain can be measured. Additionally, dynamic exercise predominantly increases preload, while isometric (static) exercise elevates afterload on the LV¹⁴. However, the response to these different loading patterns have not been previously assessed in the same individuals, which is of importance considering comparisons in the cardiovascular responses during exercise are frequently made between dynamic and static modalities. Accordingly, the present study aimed to investigate the influence of incremental dynamic cycling and isometric knee extension on LV regional and global circumferential strain. It was hypothesized that; (1) GCS would increase incrementally during cycling, mediated through increased ACS. (2) Both BCS and ACS would initially decrease during isometric exercise and as a result, would decrease GCS.

2. METHODS

2.1 Study design and population

Twenty-seven healthy males (18-40 years) of differing exercise habits (runners n=8; triathletes n=9; resistance exercisers, n=5 and no regular habits, n= 5) were recruited for this cross-sectional study. A medical questionnaire was used to exclude a past history or known current diagnosis of coronary heart disease, hypertension, diabetes mellitus, myocardial infarction, peripheral artery disease or sudden cardiac death in immediate family members. Participants were required to avoid vigorous physical activity, and consumption of alcohol (24 hours) and caffeine (12 hours) prior to data collection. Before initiation of this study, the local university ethics committee reviewed and approved the protocol which was conducted in accordance with the declaration of Helsinki. The participants in the present study are the same population as reported in our previous publication ¹⁵. Further, all methods have been fully detailed previously ¹⁵, however, a synopsis of measurement procedures and experimental protocols are provided below.

2.2 Protocol and experimental procedures

Participants attended the Sport Science Laboratories twice at the same time of day with each visit separated by at least 24 hours, but <7 days. Demographic information, physiological assessment and a baseline (resting) echocardiographic assessment were collected/completed on the first visit. During visit 2 each participant completed submaximal cycling and isometric knee extension protocols to obtain circumferential strain data during exercise.

After 5 min supine rest, heart rate (HR) (FS1, Polar Electro Oy, Kempele, Finland), systolic (SBP) and diastolic blood pressures (DBP), using manual sphygmomanometry, were recorded and used to calculate rate-pressure product, as $HR \times SBP$ and mean arterial pressure (MAP) ¹⁶. After a resting echocardiographic examination, participants completed an

incremental exercise test to exhaustion on a dedicated semi-supine ergometer (eBike-L, ergoline GmbH, GE Healthcare) using breath-by-breath expired gas analysis using a ergospirometer (Metalyser 3B, Cortex, Germany). Work rate maximum (W_{\max}) was calculated using the equation: $W_{\max} = W_{\text{com}} + \left(\frac{t}{60}\right) \times W^{17}$. We elected to use 30% and 60% W_{\max} to enable a doubling of exercise workload while ensuring an exercise intensity with suitable image acquisition.

2.3 Cycle ergometry and isometric knee extension protocols

Following a 10 min rest on the semi-supine (45°) ergometer (eBike-L, ergoline GmbH, GE Healthcare), participants performed incremental exercise of 2 x 5 min stages at 30% and 60% W_{\max} and echocardiographic images were collected during the last 3 min of each stage. HR and manual blood pressures were recorded at the end of, yet before, the termination of each exercise stage.

After 10 min seated rest, participants lay fully supine on an isokinetic dynamometer (Kin-Com 125E Plus, Chattecx Corporation, Chattanooga, USA). A full supine position was used to enable optimal echocardiographic image acquisition. The dominant leg was used for all isometric contractions of the quadriceps, which were performed at a fixed knee extension angle of 130° with the knee joint centre was aligned with the axis of the dynamometer crank arm¹⁸. A warm-up of 5-10 submaximal isometric contractions was performed prior to the maximal voluntary contraction (MVC) assessment, which was determined from the greatest of 3 maximal isometric contraction attempts interspersed with a 1 min recovery¹⁹. Following 5 min rest, participants completed an incremental protocol consisting 2 x 15s isometric contractions, separated by 2 min passive recovery, at both intensities corresponding to 40% and 75% MVC. An initial intensity of 40% MVC was chosen to match that of a previous isometric hand-grip study²⁰ and an upper intensity of 75% MVC chosen as the highest relative

intensity while attempting to limit the Valsalva manoeuvre. At the termination of contraction, five cardiac cycles, HR and manual blood pressures were recorded.

2.4 Echocardiography

All participants underwent two-dimensional transthoracic echocardiographic examinations at rest in the left lateral decubitus position and during both exercise modalities using commercially available ultrasound equipment (Vivid 7, GE Medical, London) with a phased array transducer (3S 1.4-3.8 MHz). Image acquisition and measurement procedures were conducted by the same investigator (AB) and were done so in accordance with established guidelines ^{21–23}. Five cardiac cycles were obtained at end-expiration, with the resulting data analysis from a minimum of 2 consecutive cycles when 3 were not available. Conventional parameters at rest included LV structure, systolic and diastolic function.

2.5 Speckle tracking derived circumferential strain

Circumferential strain was measured at rest and during both submaximal cycling and isometric knee extension protocols. Resting data obtained during visit 1 were used to compare with both the cycling and isometric exercise protocols. Frame rate ranged between 70 – 80 frames per second which was consistent within each individual across all conditions and also the same for apical and basal image acquisition. Using the parasternal short-axis view, the basal level was determined as the highest imaging plane at which full myocardial thickness was present with the observation of surrounding mitral valve at end-systole and positioned as circular as possible with no visible papillary muscles ²⁰. Apical images were captured proximal to the end-systolic luminal obliteration of the LV cavity with as much accuracy as possible ²⁴.

Images were analysed offline using semi-automated software (EchoPac software, GE Healthcare, UK) by one investigator. After manual endocardial border detection, the region of

interest was first automatically and then manually adjusted until the epicardal border was correctly aligned to encompass the entire LV wall thickness whilst avoiding the echogenic pericardium²²²³²². ACS and BCS were recorded as the peak value, reflective of mid-layer strain, from the average of all fully tracked myocardial segments, with GCS then calculated as the average of BCS and ACS.

The quality of echocardiographic images obtained during exercise, in addition to the grading system employed have been reported previously¹⁵.

2.6 Intra-observer reproducibility

Intra-observer reproducibility (coefficients of variation (CV)) was determined within-day at rest and between-day during both dynamic cycling and isometric knee extension exercise (Table 1). CV was calculated for each individual between trial 1 and trial 2 using the calculation: $CV = \left(\frac{\text{standard deviation}}{\text{mean}} \right) \times 100$. An average of each individual CV was then obtained to determine a global CV.

A separate cohort of 14 participants rested for 5 min in the supine position, two echocardiographic examination were performed 5 min apart. During both cycling (n=12) and knee extension (n=12) exercise, participants attended twice at the same time of day within 7 days of each other. Similar to the main data collection, participants were asked to abstain from vigorous physical activity and alcohol for 24 hours and caffeine for 12 hours prior to testing. The submaximal cycling consisted of 2 x 4 min bouts corresponding to 70 watts and 170 watts. Basal and apical images were collected at the end of each bout with image acquisition as described in section, '*Speckle tracking derived circumferential strain*'. The isometric knee extension exercise was performed as described in section, '*Cycle ergometry and isometric knee extension protocols*', with images collected at 40% and 75% MVC.

INSERT TABLE 1 NEAR HERE**2.7 Statistical analysis**

Data presented as means \pm standard deviation or median (interquartile range). Normality of data distribution was assessed by Shapiro-Wilks test. For normally distributed data, haemodynamic measures and circumferential strains assessed during exercise were compared using one-way repeated measures analysis of variance (ANOVA) with post hoc Bonferroni correction. For non-normally distributed data a Friedman test was employed followed by Wilcoxon signed-rank test to test for pairwise comparisons. A manual Bonferroni correction was applied to non-parametric tests to ensure accurate interpretation of potential statistically significant differences. All analyses were conducted using SPSS (Version 21; IBM Company, SPSS Inc., Chicago, USA) and statistical significance granted at $p \leq 0.05$.

3. RESULTS**3.1 Participant numbers for echocardiography**

All participants completed the full protocol and echocardiographic data was determined in all participants at rest. However, cardiac images during all exercise conditions could not be obtained for one participant leading to exclusion from the study, resulting in a total sample of twenty-six participants available for statistical analyses. Participant characteristics and resting left ventricular structure, systolic and diastolic function are presented in table 2. Furthermore, due to poor image quality, circumferential strain data were not acquired during cycling at 30% W_{\max} ($n = 2$) and 60% W_{\max} ($n = 3$) and during knee extension at 75% MVC ($n = 3$). Consequently, 22 and 23 participants were included during cycling and knee extension, respectively. The reasons for missing data for blood pressure have been detailed previously¹⁵.

INSERT TABLE 2 NEAR HERE

3.2 Maximal physiological and haemodynamic parameters

Following the maximal incremental exercise test and MVC, group physiological parameters were: $\dot{V}O_{\text{peak}}$ (n=25) $46.1 \pm 12.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, W_{max} $277 \pm 49 \text{ W}$; 30% W_{max} $83 \pm 15 \text{ W}$; 60% W_{max} , $166 \pm 29 \text{ W}$; MVC, $1103 \pm 267 \text{ N}$; 40% MVC, $441 \pm 107 \text{ N}$ and 75% MVC, $828 \pm 200 \text{ N}$. All haemodynamic data during cycling and knee extension are presented in Table 3. HR, SBP, DBP, MAP and RPP significantly (all $p < 0.01$) increased with progressive exercise intensity from rest during both cycling and knee extension exercises.

INSERT TABLE 3 NEAR HERE

3.3 Circumferential strain during exercise

LV GCS, ACS and BCS during cycling and isometric exercise are presented in Figure 1a-b. During semi-supine dynamic cycling, GCS increased from rest ($-22.85 \pm 3.26\%$) to 30% W_{max} ($-27.17 \pm 4.63\%$, $p = 0.002$) and then further increased to 60% W_{max} ($-29.87 \pm 2.59\%$, $p = 0.031$). ACS increased from rest ($-26.29 \pm 4.84\%$, $p < 0.001$) to 30% W_{max} ($-36.84 \pm 6.94\%$) and then remained unchanged to 60% W_{max} ($-40.72 \pm 4.06\%$, $p = 0.068$). In contrast, there was a statistically significant decrease in BCS from rest ($-19.41 \pm 2.79\%$) to 30% W_{max} ($-17.51 \pm 4.66\%$, $p = 0.049$) which then remained statistically unchanged thereafter to 60% W_{max} ($-19.03 \pm 4.14\%$, $p = 0.506$).

During isometric knee extension, GCS decreased from rest ($-22.63 \pm 3.46\%$) to 40% MVC ($-20.10 \pm 2.78\%$, $p = 0.031$) and then remained unchanged to 75% MVC ($-19.72 \pm$

2.91%, $p = 1.00$). Similarly, BCS decreased from rest ($-19.21 \pm 2.58\%$) to 40% MVC ($-13.55 \pm 3.45\%$, $p < 0.001$) and then remained unchanged to 75% MVC ($-12.21 \pm 2.89\%$, $p = 0.162$), whereas ACS did not change with exercise intensity (rest, $-26.05 \pm 5.34\%$; 40% MVC, $-26.64 \pm 4.53\%$ and 75% MVC $-27.22 \pm 5.34\%$, all $p = 1.00$).

INSERT FIGURE 1 NEAR HERE

4. DISCUSSION

This study is the first to investigate the influence of both incremental dynamic and static (isometric) exercises on LV global and regional circumferential strain in the same participants. Accordingly, the principle findings were that, (1) during dynamic and static exercise, opposing GCS responses were observed. During aerobic exercise, there was a stepwise increase in GCS, whereas during the static exercise GCS decreased to 40% MVC but plateaued thereafter. In addition, the GCS responses in both exercises modalities were due to different circumferential strain mechanics. (2) During aerobic exercise, the increase in GCS was mediated by increasing ACS with trivial effects on BCS. (3) In contrast, static exercise had no effect on ACS with the GCS changes being mediated by a decrease in BCS from rest. Therefore, it appears that exercise modality plays some role in the responses of circumferential strain.

These observations present a novel finding which adds to work having been performed thus far, and at higher intensities than have previously been used, highlighting that GCS alterations are the consequence of opposing physiological responses between the basal and apical regions. Global strain provides a good indication of deformation encompassing the entire LV; apical and basal strain may compliment the global derivative (when calculated as an average of apical and basal planes) by determining the regional contributions.

4.1 Circumferential strain during semi-supine cycling

GCS increased with exercise initiation and further increased between exercise intensities which agrees with our first hypothesis. These observations concur²⁵ and contrast with prior studies, of which found no statistically significance increase between penultimate and final exercise intensities^{6,8}. Although a lack of statistical significance does not imply the changes are not biologically meaningful, the present study extends previous work and clarifies the position that beyond low-moderate intensities and up to moderate intensity cycling, GCS does not plateau. In this study, exercise intensity was greater than the absolute⁸ and relative workloads⁶ employed previously and in particular, larger intervals between workloads were used compared with the protocol of Doucende et al.⁶. Thus, discrete differences in circumferential strain may only become evident with higher intensities and/or wider categories. Moreover, Unnithan et al.⁸ used upright cycling compared to semi-supine cycling in the present study, and therefore, a postural effect during the exercise cannot be ruled out. The studied population should also be considered; Unnithan et al.⁸ used adolescents whereas we recruited adults, whether the circumferential strain response differs between adolescents and adults or are influenced by posture are intriguing prospects that may wish to be explored further.

Region-specific function was noted during cycling exercise, ACS initially increased from rest and then demonstrated a trend toward an increase between exercise intensities, which underlines the functional reserve capacity of the apex in response to cardiovascular exercise stress, whereas BCS decreased initially and was unchanged thereafter. Despite a statistically significant change in BCS following the transition of rest to exercise, the biological significance of this small reduction (~2% strain) is likely to be trivial. Although, lower basal

shortening as seen in this study compared to the apex may not necessarily reflect a lower contribution to physiological contraction²⁶. Nonetheless, from the present data, GCS (when averaged from the base and apex) is predominantly the consequence of changes within the apex during dynamic exercise and are similar to previous studies having shown increased ACS, but unchanged BCS^{9,10}. In contrast, others reported a strain reserve in BCS during cycling compared with baseline¹¹ and disagrees with the present study, which is indicative of limited-to-no functional reserve, at least up to 60% W_{\max} . Pieles et al.¹¹ studied an adolescent cohort; whether younger individuals demonstrate alternate circumferential mechanics to adults during incremental exercise is difficult to determine since ACS was not reported, whereby preventing a direct comparison; yet, as alluded to previously, such possibilities of an age-dependant response require future study.

4.2 Circumferential strain during isometric knee extension

During incremental isometric knee extension exercise, GCS reduced from rest to 40% MVC and then remained unaltered to 75% MVC, which is in agreement with our second hypothesis. The reduction in GCS concurs with previous reports utilising upper-body isometric hand-grip exercises^{7,12} and suggests the GCS responses during upper and lower body based isometric exercise are independent of the exercise modality. Similar to the cycling exercise, we found regional differences in circumferential strain between the apex and base. However, unlike during dynamic exercise, ACS remained unchanged through the incremental protocol while BCS was reduced. These observations are in partial agreement with our second hypothesis, with respect to BCS, yet are at odds in regards to the responses observed at the apex. The regional BCS responses during isometric exercise are similar to another study having used incremental resistance exercise¹³. In contrast, ACS was reduced in their study but unchanged

in ours and the reasons for this disagreement are unknown at present. A supine unilateral knee extension was performed in this study, whereas Stohr et al.¹³ used a seated double-leg press held isometrically (90° knee flexion) for a short duration following a near-complete leg extension. Blood pressure during their experimental protocol^{13,27} far exceeded those of the present; the larger work required to perform the resistance exercise even at similar relative workloads would have accentuated the afterload exposure. Nonetheless, this does suggest that changes in BCS are consistent across a broad range of afterloads and, may be more sensitive to small increases in afterload than ACS.

Although we can only speculate on the responsible mechanisms for the global and regional observations herein, changes in fibre length during the isometric exercise may adversely affect the ensuing shortening and tension developed and as a consequence LV function²⁰. The unique myocardial fibre orientation should also be considered and in addition to a circumferential strain basal-to-apical gradient, an epicardial-to-endocardial strain gradient exists in both basal and apical regions⁵; examination of such layers may provide further insight.

The implications of an immediate reduction in GCS and BCS remain to be explored and more so, the magnitude of reduction required before it can be considered biologically important (e.g. it significantly alters LV output and thus cardiac performance) is yet to be fully elucidated. However, Stohr et al.¹³ identified only transient reductions following a restoration to baseline levels during recovery intervals. The long-term ramifications of repeated bouts and exposure to transient reductions in circumferential strain over multiple years are unknown. GCS was significantly reduced in resistance trained athletes compared with normal controls^{28,29}, yet more studies are required in those who perform repetitive resistance exercise for both competition (i.e. highly trained athletes) and recreation.

4.3 Limitations

We have previously acknowledged the experimental protocol limitations¹⁵, with regards to the potential error of the blood pressure measurements and the confirmation of afterload exposures. Also, we included only young, healthy males so the findings of this study may not reflect the entire population such as females, older aged individuals or special clinical populations. At rest images were obtained in the supine position, whereas during cycling they were collected in the semi-supine position. However, despite a reduction in LV preload following a transition from supine to head-up tilt position, LV circumferential strain was comparable between body positions³⁰. Thus, the physiological increases in regional and global circumferential strain observed in this study, during dynamic exercise, are unlikely to be attributed to the differences in resting and exercising body positions when acquiring echocardiographic images.

Technical limitations of echocardiography are especially pertinent when acquiring the basal and apical imaging planes. First, with two-dimensional echocardiography basal and apical images are obtained within different heart beats and thus in this study, obtained during two separate contractions during the isometric knee extension. Second, obtaining the consistent imaging planes is challenging which may affect intra-subject variability⁶. Indeed this intrinsic limitation of two-dimensional imaging may be overcome with the use of three-dimensional which facilitates the detection of deformation in and out of plane^{4,22}. Nevertheless, the resting within-day intra-observer reproducibility reported in this study are consistent with previous reports^{8,31}. As would be anticipated, the CV were greater during both dynamic and static exercises compared with rest, yet were similar to another incremental exercise study, albeit in an adolescent population and performing upright cycle ergometer exercise⁸. During isometric exercise, BCS demonstrated the largest CV which should therefore be considered when interpreting the findings of this study, especially since BCS was the largest respondent during

isometric knee extension. However, the changes in BCS from rest to 40% (29.46%) and 75% MVC (36.44%) were greater than the intra-observer CV at 40% and 75% MVC. Still it is possible that the magnitude of decrement in BCS could have been influenced by the reproducibility.

5. CONCLUSIONS

This study is the first to investigate global and region-specific circumferential strain during both incremental dynamic cycling and isometric knee extension exercises in the same participants. GCS progressively increased during dynamic exercise but decreased during short-duration isometric work. These acute, global alterations were due to apical increase during cycling, yet basal reductions during isometric knee extension. Cardiac strains, circumferentially determined, appear to be modality dependant following region-specific changes within the myocardium, concomitant with exercise stress of differing physiological demands.

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Tables

Table 1 Reproducibility of apical, basal and global circumferential strain at rest and during submaximal cycling and isometric knee extension exercise

Measure	Rest		Submaximal cycling				Isometric knee extension			
			70 watts		170 watts		40% MVC		75% MVC	
	n	CV (%)	n	CV (%)	n	CV (%)	n	CV (%)	n	CV (%)
Basal circumferential strain	13	6.31	11	11.07	8	10.84	9	15.4	10	17.28
Apical circumferential strain	12	7.93	11	8.90	8	14.35	9	11.74	9	8.71
Global circumferential strain	11	3.64	11	8.86	7	10.21	9	9.75	8	6.05

CV: coefficient of variation.

Table 2 Participant characteristics and echocardiographic left ventricular structure and conventional systolic and diastolic function (n=26).

Standard demographics	
Age (years)	30 ± 6
Height (m)	1.77 ± 0.08
Mass (kg)	75.87 ± 9.90
Left ventricular structure	
IVSd (mm)	10.23 ± 1.17
IVSs (mm)	13.08 ± 2.42
LVIDd (mm)	53.39 ± 3.85
LVIDs (mm)	36.42 ± 3.30
PWTd (mm)	9.75 ± 1.57
PWTs (mm)	15.15 ± 2.47
LVEDV (mL)	125.87 ± 26.18
LVESV (mL)	52.19 ± 12.27
LVM (g)	204.16 ± 37.04
LVMi (g/m ²)	106.16 ± 19.77
RWT	0.37 ± 0.06
Left ventricular systolic Function	
EF (%)	58.39 ± 5.36
SV (mL)	73.68 ± 17.04
\dot{Q} (L·min ⁻¹)	4.22 ± 0.76
Lateral S' (cm·s ⁻¹)	12.92 ± 1.94
Septal S' (cm·s ⁻¹)	9.23 ± 1.14
Left ventricular diastolic Function	
E-wave (cm·s ⁻¹)	72.23 ± 9.57
A-wave (cm·s ⁻¹)	37.19 ± 7.33
E/A Ratio	2.02 ± 0.51
DT (ms)	259.82 ± 62.94
Lateral E' (cm·s ⁻¹)	18.54 ± 3.00
Septal E' (cm·s ⁻¹)	12.46 ± 1.98
Lateral A' (cm·s ⁻¹)	7.92 ± 1.87

Septal A' (cm·s ⁻¹)	7.96 ± 1.61
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Data are means ± standard deviation.

d: end-diastole; s: end-systole; IVS: interventricular septum; LVID: left ventricular internal diameter; PWT: posterior wall thickness; LVEDV: left ventricular end-diastolic volume; LVESV: left ventricular end-systolic volume; LVM: left ventricular mass; LVMi: left ventricular mass index; RWT: relative wall thickness; EF ejection fraction; SV stroke volume; \dot{Q} : cardiac output; S': Tissue Doppler systolic velocity; E: mitral inflow early diastolic velocity; A: mitral inflow late diastolic velocity; E/A: ratio between early and late diastolic mitral inflow velocities; DT: deceleration time; E': tissue Doppler early diastolic velocity; A': tissue Doppler late diastolic velocity.

All data have been reported previously ¹⁵.

Table 3 Haemodynamic measures at rest and during both intensities of the cycling and isometric knee extension exercises

Variable	Cycling (% W_{\max})			Knee extension (% MVC)		
	Rest	30%	60%	Rest	40%	75%
HR (beats·min ⁻¹)	57 (14)	96 (11) †	128 (14) †‡	57 (14)	81 (24) †	97 (29) †‡
SBP (mmHg) ^a	118 ± 9	141 ± 9 †	172 ± 21 †‡	118 ± 9	130 ± 10 †	146 ± 18 †‡
DBP (mmHg) ^{b c}	77 (9)	81 (4) †	82 (6) †‡	77 (9)	79 (9) †	82 (9) †‡
MAP (mmHg) ^{b c}	89 ± 6	101 ± 5 †	114 ± 8 †‡	89 (11)	94 (5) †	104 (10) †‡
RPP ^a	6867.00	13100.00	22862.00	6867.00	10664.00	13774.00
(beats·min ⁻¹ · mmHg)	(1652.00)	(2617.50) †	(3540.50) †‡	(1652.00)	(3897.50) †	(4577.50) †‡

Normally distributed data presented as mean ± standard deviation, non-normally distributed data presented as median (interquartile range)

HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; RPP: rate pressure product; W_{\max} : work rate maximum; MVC: maximal voluntary isometric contraction.

† $p < 0.01$ compared to rest.

‡ $p < 0.01$ compared to previous intensity.

^a $n = 25$ during cycling and knee extension ^b $n = 25$ during cycling, ^c $n = 24$ during knee extension.

All data except RPP have been reported previously ¹⁵.

Figure captions

Figure 1 Circumferential strain during incremental cycling ($n=22$) (**a**) and during incremental isometric knee extension ($n=23$) (**b**).

ACS: apical circumferential strain; BCS: basal circumferential strain; GCS: global circumferential strain; W_{\max} : work rate maximum; MVC: maximum voluntary contraction.

† $p < 0.05$ compared with rest

‡ $p < 0.05$ compared with previous intensity

See text for exact p values. Data are presented as means \pm standard deviation